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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,285	01/15/2001	Nicholas C. Nicolaides	MOR-0017	2664

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EXAMINER

NGUYEN, DAVE TRONG

ART UNIT PAPER NUMBER

1632

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/760,285

Applicant(s)

NICOLAIDES ET AL.

Examiner

Dave T. Nguyen

Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 November 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-20,22-26 and 32-84 is/are pending in the application.
- 4a) Of the above claim(s) 14-20,25,32-67,69 and 71 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1,4-13,22 and 72-84 is/are allowed.
- 6) ☒ Claim(s) 23,24,26,68 and 70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Claim 23 has been amended, claims 21, 27-31, and 83 have been canceled, and claim 84 has been added by the amendment filed November 5, 2004.

Claims 14-20, 25, 32-67, 69, 71 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected claimed invention. A complete response to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) MPEP 821.01.

Elected claims 1, 4-13, 22-24, 26, 68, 70, 72-84 readable on the elected invention are pending for examination.

The finality of the previous office action has been vacated by the examiner, particularly in view of the first paragraph as set forth on page 10 of the previously stated office action. As such, the cover letter of the previously stated non-final office action, which states that the office action is the final office action, is incorrect. The examiner acknowledges the interview held by Attorney Felicity Groth and the examiner regarding the typographical error as appeared on the cover letter of the office action dated July 13, 2004.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The rejection under 35 USC 102(b) as being anticipated by, on the alternative, under 35 USC 103 as being unpatentable over Cerniglia (Appl. Environ. Microbiol. 56,

3, 661-668, 1990) or LaVoie, Carcinogenesis, Vol. 6, pp. 1483-1488, 1985, is withdrawn by the examiner because of applicant's response dated Nov 7, 2004.

The rejection under 35 USC 103(a) as being unpatentable over any of LaVoie, Carcinogenesis, Vol. 6, pp. 1483-1488, 1985, taken with any of Krahn, Wigley and Slaga, and further in view of Chakravarti *et al.* (PNAS, Vol. 92, pp. 10422-10426, 1995), is withdrawn by the examiner.

The rejection of claims 1, 4-13, 22, and 72-83 under 35 USC 103 as being unpatentable over Euler alone or in combination with any prior art of record is withdrawn by the examiner.

Following are the remaining rejections, which include a new ground of rejection with respect to claim 24, which is now dependent from the amended claim 23. This new ground of rejection is necessitated by the amendment to claim 23.

Claim 23 remains rejected under 35 USC 103, as being unpatentable over Euler (Caplus Database, AN: 1948:32360, abstract only).

The claims are readable on an assay of detecting a phenotype on plant seeds exposed to anthracene or a combination of anthracenes and additional anthracene or other mutagens, wherein the detected phenotype is a result of a mutation of a gene in the seed.

Euler teaches that a number of genotoxic compounds such as camphor, anthracene, and benzoquinone are effective for introducing a mutation in an endogenous gene contained in pollens, and in plants treated with these compounds, no ears of grain were developed.

With respect to an elected anthracene for examination, it would also have been obvious for of ordinary skill in the art to as a matter of design choice or minor modifications to employ any known anthracene including those elected anthracenes as claimed in the assay employed in Euler. One of ordinary skill in the art would have been motivated to employ any known anthracene or a combination of anthracene compounds or known mutagenic compounds simply because of its equivalent effect or combination effect, respectively, in generating a diminished catalase activity in treated plants.

Thus, the claimed invention was *prima facie* obvious.

Claims 23, 68, 70 remain rejected under 35 USC 103 as being unpatentable over unpatentable over Euler (Caplus Database, AN: 1948:32360, abstract only) taken with Kimm (Korean J. of Biochemistry, 1982, Vol. 14, No. 1, pp. 1-8, abstract), and Laduca, Diss, Abstr Int [B], 55, 11, 4741, 1995, Database CancerLit.

To the extent that Euler does not teach an administration of additional environmental carcinogens such as MNNG and NMU, Kimm teaches that these environmental carcinogens are effective for generating a mutation in vegetables. Thus, it would have been obvious for one of ordinary skill in the art to employ an additional mutagen such as MMNG or NMU in the method of Euler as a matter of increasing a combination effect and reducing the time needed for a mutation or mutational phenotype to occur. One would have expected such since Euler teaches that plants treated with a mutagenic chemical compound all produce no ears of grains.

Thus, the claimed invention was *prima facie* obvious.

Claims 23-24 are rejected under 35 USC 103(a) as being unpatentable over Euler (Caplus Database, AN: 1948:32360, abstract only) taken with Chakravarti *et al.* (PNAS, Vol. 92, pp. 10422-10426, 1995).

The claims are readable on an assay of detecting a phenotype on plant seeds exposed to anthracene or a combination of anthracenes and additional anthracene or other mutagens, wherein the detected phenotype is a result of a mutation of a gene in the seed.

Euler teaches that a number of genotoxic compounds such as camphor, anthracene, and benzoquinone are effective for introducing a mutation in an endogenous gene contained in pollens, and in plants treated with these compounds, no ears of grain were developed. Euler specifically states that the "genes responsible for the formation of the porphyrins must then be inactivated" (emphasis added).

With respect to an elected anthracene for examination, it would also have been obvious for of ordinary skill in the art to as a matter of design choice or minor modifications to employ any known anthracene including those elected anthracenes as claimed in the assay employed in Euler. One of ordinary skill in the art would have been motivated to employ any known anthracene or a combination of anthracene compounds or known mutagenic compounds simply because of its equivalent effect or

Art Unit: 1632

combination effect, respectively, in generating a diminished catalase activity in treated plants.

With respect to the limitation of employing an assay to test whether or not a mutation has occurred in a gene of interest as the result of the effect of a chosen anthracene, wherein the limitation is not taught by Euler, Chakravarti teaches that such assays are conventional and routine in the prior art to assay for the effect of gene expression in the presence of an anthracene chosen for the mutation assay, Chakravarti, page 10422, and page 10423.

Thus, it would have been obvious for one of ordinary skill in the art to employ a gene report assay to determine the sensitivity and reproducibility of results due to exposure of tested cells to a chosen anthracene such as 9/10, dimethylantracene. One of ordinary skill in the art would have been motivated to employ any gene reporter assay known in the prior art in the mutation analysis method employed in the combined cited references because Chakravarti do teach that such assays are conventional and routine in the prior art to assay for the effect of gene expression in the presence of an anthracene chosen for the mutation assay, and because such incorporation of reporter gene expression assays would enhance the sensitivity and reproducibility of results due to exposure of tested cells to a chosen anthracene such as 9/10, dimethylantracene.

Thus, the claimed invention as a whole, was *prima facie* obvious.

Claims 23, 24, 26, 68 are rejected under 35 USC 103(a) as being unpatentable over any of Euler (Caplus Database, AN: 1948:32360, abstract only) taken with Zhang (US 20002/0064879 A1).

Euler teaches that a number of genotoxic compounds such as camphor, anthracene, and benzoquinone are effective for introducing a mutation in an endogenous gene contained in pollens, and in plants treated with these compounds, no ears of grain were developed. Euler specifically states that the “genes responsible for the formation of the porphyrins must then be inactivated” (emphasis added).

With respect to an elected anthracene for examination, it would also have been obvious for of ordinary skill in the art to as a matter of design choice or minor modifications to employ any known anthracene including those elected anthracenes as claimed in the assay employed in Euler. One of ordinary skill in the art would have been motivated to employ any known anthracene or a combination of anthracene compounds or known mutagenic compounds simply because of its equivalent effect or combination effect, respectively, in generating a diminished catalase activity in treated plants. Euler does not teach explicitly that 1,2-dimethylantracene induces genotoxic activities in any cell *in vitro* or *in vivo*.

However, at the time the invention was made, Zhang teaches a method for obtaining a plant with a genetic lesion in a gene sequence flanked in a wild type chromosome by known polynucleotide sequences, comprising exposing the plant and cells thereof to a mutagenic chemical substance. For example, a DNA binding assay was also disclosed in Zhang to determine the presence the mutant gene sequence.

Thus, it would have been obvious for one of ordinary skill in the art to employ a binding assay for detecting the presence of a mutation in a gene(s) in the method of Euler. One would have been motivated to do so because Euler teaches that anthracene is a potent chemical mutagen for inducing random mutation in gene sequence, thereby resulting in a detectable phenotype in a plant or parts thereof, and an mutation assay as disclosed in Zhang would provide one of ordinary skill in the art c convenient tool to analyze the presence of such mutation in a gene sequence contained in the pollens of Euler.

To the extent that the claims are readable on the step of removing the carcinogens and/or mutagens from the medium prior to the analysis step, the claims are also obvious over the cited prior art because one of ordinary skill in the art would have been motivated to do the same in order to monitor the exposing time of carcinogens to the cells.

Thus, the claimed invention was as a whole *prima facie* obvious.

Applicant's response (Nov 7, 2004, bottom of page 15, page 16 through page 17, and last par. of page 18) has been considered by the examiner but is not found persuasive for the reasons as set forth in the rejections, and for the following reasons:

On the bottom of page 15, applicant asserts that due to the definition of "hypermutable" as the state in which a cell is made more susceptible to mutation through the loss or impairment of the mismatch repair system, Euler is not a prior art against the claimed invention because Euler does not teach hypermutability of the chemically treated pollen grain. The argument is not persuasive because Euler

Art Unit: 1632

specifically teaches that in plants treated with mutagenic anthracene, no ears of grain were developed, and that "genes responsible for the formation of the porphyrins must then be inactivated" (emphasis added). As the result of the teaching of Euler coupled with the well-established fact about anthracene being a genotoxic compound (see the as-filed specification, and LaVoie), it would necessarily flow from the teaching of Euler that anthracenes cause a mutation in a gene of interest (in this case, mutation of genes responsible for the formation of the porphyrins). Claim 23 does not recite the limitation of "hypermutable" as asserted by applicants. Applicant further argues that due to the disclosure in Example 3 as provided by the specification Euler does not teach that anthracene is a chemical inhibitor of a mismatch repair gene, the examiner reiterates that claims 23, and claims dependent therefrom do recite such limitation, and thus, the rejections are maintained for the reasons of record.

Claims 1, 4-13, 22, and 72-84 are in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

Art Unit: 1632

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **571-272-0731**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Amy Nelson*, may be reached at **571-272-0804**.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center number, which is **703-872-9306**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632


DAVE T. NGUYEN
PRIMARY EXAMINER